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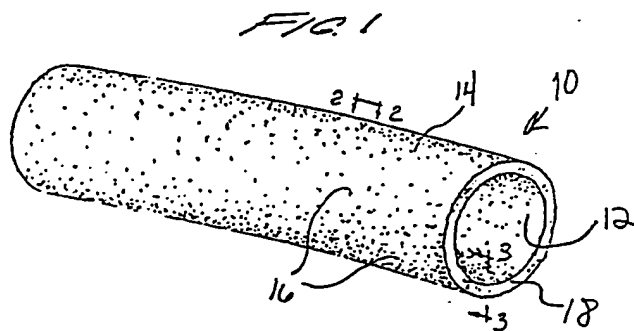
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(54) Cardiovascular graft and method forming same.

(57) The method for forming a biocompatible polymer graft particularly adapted for cardiovascular use comprises the steps of: choosing a suitable, non-solvent, two component, hydrophilic or hydrophobic biocompatible polymer system from which the graft may be formed; choosing a suitable water soluble inorganic salt to be compounded with the biocompatible polymer system; grinding the salt crystals and passing same through a sieve having a pre-determined mesh size; drying the salt crystals; compounding the salt crystals with the biocompatible polymer system; forming a tube from said compounded salt and polymer system by reaction injection or cast molding; and leaching the salt crystals from the formed tube with water, said leaching of said salt crystals providing a tube with a network of interconnecting cells formed in the area from which the salt crystals have been leached.

Further, according to the present invention, there is also provided a graft particularly adapted for cardiovascular use, said graft comprising a tube which has been reaction injection molded, cast molded, or extruded from a non-solvent, two component hydrophilic or hydrophobic biocompatible polymer system and which has a honeycomb of interconnecting cells throughout the thickness of its wall formed by the leaching of a compounded inorganic salt therefrom.



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5 CARDIOVASCULAR GRAFT AND METHOD OF FORMING SAME

BACKGROUND OF THE INVENTION

Field of the Invention

- 10 The present invention relates to a cardiovascular graft and a method of forming same. More particularly, the invention relates to a cardiovascular graft fabricated of a porous, biocompatible polymer system which provides for cellular ingrowth and/or increased flexibility..
- 15 The method of forming the graft utilizes a non-solvent, two component, hydrophilic or hydrophobic polymer system.

Description of the Prior Art

- 20 Heretofore various porous graft structures and methods of forming same have been proposed.

Two such graft structures and methods for their formation are disclosed in the following U.S. Patent:

25	<u>U.S. PATENT NO.</u>	<u>PATENTEE</u>
	4,334,327	Lyman
	4,355,426	MacGregor

- 30 The Lyman U.S. Patent No. 4,334,327 discloses a flexible ureteral prosthesis (graft) fabricated from copolyurethane materials. The prosthesis includes an elongate duct having a lumen whose interior surface is ultrasmooth to impede incrustation. An external cuff, formed of a foam-like material, is formed around a portion of
- 35 the elongate duct. The cuff has at least 40 % void

1 space therein which provides a proper density for receiving  
sutures to enable fixation of the cuff by suturing to  
appropriate muscular tissue. The inner diameter of the  
prosthesis must be conformed to the outer diameter of  
5 the ureter of the recipient. Further, the prosthesis  
is provided with a one-way valve to prevent backflow of  
urine.

The process of formation of the prosthesis involves  
10 selecting a tubular mandrel having a highly polished  
surface and an outer diameter corresponding to a desired  
inner diameter for the prosthesis. One end of the mandrel  
is configured to conform to a cavity shape which is  
of acceptable size for forming the body of the one-  
15 way valve.

The next step in this process involves applying a fluid  
layer of block copolymer to the mandrel. The block  
copolymers found particularly suitable as ureter replace-  
20 ment materials include copolyurethanes, copolyether-  
urethanes and/or copolyether-urethane-ureas. With the  
mandrel suitable coated, the copolymer layer is solidified  
to fix its shape into conformance with the mandrel  
surface. Mold blocks are then secured around terminal  
25 segments at each end of the coated mandrel to form  
boundaries for the formation of an exterior cuff. These  
blocks have an opening centrally disposed therein  
corresponding to an approximate diameter of the coated  
mandrel to facilitate mounting of the mandrel within  
30 the respective mold blocks. The cuff is then formed  
by permanently affixing a material whose final state  
develops a foam-like composition over the coated mandrel  
between the mold blocks. Once the cuff is formed and  
appropriately configured to facilitate suturing to  
35 fascia within the patient, the mold blocks are removed

1 and the mandrel withdrawn. The foam like end product  
structure may be fabricated by admixing powdered inorganic  
salt to a solution of approximately 12 % to 17 % (w)  
block copolymer or may utilize a fluid transfer method  
5 for establishing the voids throughout the cuff material.

The MacGregor U.S. Patent No. 4,355,426 discloses a  
cardiovascular prosthetic device comprising a porous  
surface and a network of interconnected interstitial  
10 pores below the surface of the device in fluid flow  
communication with the surface pores.

Several other devices are disclosed which fall broadly  
into two classes, rigid items and flexible polymeric  
15 items.

The flexible porous polymeric grafts are formed from  
a segmented polyurethane and more preferably a segmented  
hydrophilic polyurethane. The graft may be provided  
with a porous surface and subsurface network on a coherent  
20 substrate or may be formed as a wholly porous structure.

Various specific structural embodiments of flexible  
graft are dependent upon the function the graft is to  
serve, as disclosed in the MacGregor patent.

25 Further, MacGregor proposes several different procedures  
for forming the various graft structures defined, all  
of which require the use of a polymer resin and a solvent.

30 As described above, the prior methodology of formation  
of graft structures has involved the mixing of water  
soluble inorganic salts into polymer-solvent systems  
and then forming a graft of a desired but limited thick-  
ness by one of many procedures available. The resulting  
35 polymer network is then cured and leached of salt by  
soaking in an aqueous solution.

- 1 Also, foaming agents and blowing agents have been used  
to produce "pseudo-porous grafts", i.e., to produce  
a closed pore cellular structure to the graft. The  
pore sizes are often irregular and difficult to control  
5 and can be larger than the 200 micron maximum size  
recommended for tissue ingrowth. Further, the by-  
products of the foaming reaction can be physiologically  
damaging.
- 10 Additionally, use of mandrel dipping methods results  
in grafts which are limited to simple, thin-walled grafting  
material with reproducibility and uniformity being  
unattainable.
- 15 As will be described in greater detail hereinafter,  
the graft and method of the present invention have  
a number of advantages over the prior art grafts and  
methods, such advantages including a simple method  
of formation using a nonsolvent polymer system, ease  
20 of reproducibility of the exact graft structure, uniformi-  
ty of the porous network within the graft while allowing  
for variable porosity and variable wall thickness  
of the graft, and the use of hydrophobic as well as  
hydrophilic materials in the production of the graft.

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#### SUMMARY OF THE INVENTION

- According to the present invention, there is provided  
a method for forming a biocompatible polymer graft  
30 particularly adapted for cardiovascular use, said  
method comprising the steps of: choosing a suitable,  
non-solvent, tow component, hydrophilic or hydrophobic  
biocompatible polymer system from which the graft may  
be formed; choosing a suitable water soluble inorganic  
35 salt to be compounded with the biocompatible polymer

1 system; grinding the salt crystals and passing same  
through a sieve having a predetermined mesh size; drying  
the salt crystals; compounding the salt crystals with  
the biocompatible polymer system; forming a tube from  
5 said compounded salt and polymer system by reaction  
injection or cast molding; and leaching the salt crystals  
from the formed tube with water, said leaching of said  
salt crystals providing a tube with a network of inter-  
connecting cells formed in the area from which the  
10 sale crystals have been leached.

Further, according to the present invention, there  
is also provided a graft particularly adapted for cardio-  
vascular use, said graft comprising a tube which has  
15 been reaction injection molded, cast molded, or extruded  
from a non-solvent, two component hydrophilic or hydro-  
phobic biocompatible polymer system and which has a  
honeycomb of interconnecting cells throughout the thick-  
ness of its wall formed by the leaching of a compounded  
20 inorganic salt therefrom.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a perspective view of the cardiovascular  
graft of the present invention.

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Fig. 2 is a magnified view in section of the outer  
surface of a section of the graft taken along line  
2-2 of Fig. 1 and shows the porous nature of the surface  
of the graft.

30

Fig. 3 is an enlarged cross-sectional view of the graft  
wall, is taken along line 3-3 of Fig. 1 and shows the  
honeycomb configuration of the pores throughout the  
thickness of the graft wall.

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## 1 DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings in greater detail, there is illustrated in Fig. 1 a graft 10, particularly adapted for cardiovascular use. As illustrated, the graft 10 has a tubular configuration within an inner surface 12 and an outer surface 14 and is formed of a porous biocompatible polymer material with the surfaces 12 and 14 having cells or pores 16 therein.

10 Referring now to Fig. 2, there is illustrated therein a magnified view of the outer surface 14 of the graft 10 of the present invention and is taken along line 2-2 of Fig. 1.

15 This magnified view of the outer surface 14 shows that the pores 16 are all substantially uniform. However, the diameter of these pores 16 may vary from graft to graft as dictated by the location at which the graft 20 10 is to be used within the cardiovascular system. For example, if the graft 10 were to be positioned in a popliteal artery, the pore diameter would be larger than the pore diameter of a graft 10 that would be used in say, an area such as the hand. Regardless of 25 the site of use of the graft 10, the diameter of the pores 16 within each particular graft will remain constant and uniform.

It has been found through empirical studies that the 30 diameter of these pores or cells 16 may range from 1 micron to 200 microns and still allow for fixation of the graft to tissue underlying the area in which the graft 10 is to be positioned. In this respect, the diameter range has been found useful in that a 35 suture placed through the graft 10 will be easily fed

1 through the graft material at one range extreme which  
at the other range extreme, the porosity is not great  
enough to allow for tearing of the graft material when  
a suture is passed through same.

5

Referring now to Fig. 3, there is illustrated therein  
a cross-sectional microscopic view through the wall  
18 of the graft 10 of the present invention which is  
taken along line 3-3 of Fig. 1. In this view is illustrat-  
10 ed the honeycomb arrangement of the cells or pores  
16. In this respect, by forming the graft 10 by the  
method of the present invention, the cells or pores  
16 within the graft are formed so that they interconnect  
throughout the wall thickness to form a porous network  
15 through the wall 18 of the graft 10. This honeycomb  
network arrangement in a porous biocompatible polymer  
facilitates diffusion of nutrient-containing tissue  
into the interconnecting cells 16. Further, with a  
maximum pore size of 200 microns, cellular ingrowth  
20 is promoted to form a substrate of connective tissue  
on which a pseudointima may form. Further, the constant  
diffusion of nutrient material through the graft wall  
18 afforded by the honeycomb network prevents tissue  
necrosis along the inner surface of the cardiovascular  
25 graft 10 and prevents sloughing off of the pseudo-  
intima with an end result of an encapsulated cardio-  
vascular graft 10 with tissue filling the cells 16  
and a smooth endothelial surface forms over the inner  
surface 12 of the graft 10 over which the blood will  
30 flow.

Turning now to the method for forming the graft 10,  
it is first to be noted that the biocompatible polymer  
system from which the graft is manufactured is a two  
35 componentpolymer system including as polyurethane,



1 silicone and polytetrafluorethylene and a curing agent.  
Also, other hydrophilic or hydrophobic polymer systems  
may be utilized and the choice of materials should  
not be confined to these three polymers.

5

In such a two component polymer system, the first component  
is a resin, such as a silicone resin, and the second com-  
ponent is a curing agent/catalyst such as, for example, platinum.  
Other curing agents/catalysts available for use in  
10 such two components systems are tempered steel, heat,  
cross-linkers, gamma radiation, and ureaformaldehyde.

As described above, it will be noted that this two  
component system is a non-solvent system. That is,  
15 the two components react together in the presence of  
salt, which is compounded with the two component system  
as described below. The two components are not a polymer  
and a solvent.

20 Once an appropriate two component polymer system has  
been chosen, it is compounded with a water soluble  
inorganic salt such as, but not confined to, sodium  
chloride. The size and shape of the pores 16 of the  
honeycomb network are dictated by the choice of the  
25 specific inorganic salt that is compounded with the  
polymer system. Typically, the crystals of salt chosen  
are ground and then put through a sieve whose chosen  
mesh size corresponds to the size requirement for  
the pore diameter to be utilized in the graft 10. The  
30 salt crystals are then placed in a drying oven at 135°C  
for a period of no less than 24 hours.

The polymer system is then processed according to the  
method recommended by the manufacturer of the particular  
35 polymer system utilized and the dried salt crystals  
are mixed with the polymer system and compounded. The

1 porosity and flexibility of the graft 10 is dependent  
upon the ratio of water soluble inorganic salt to the  
polymer system with this ratio ranging anywhere from  
25-75% by weight.

5

Once compounded, the water soluble inorganic salt and  
polymer are injection molded or reaction injection  
molded to form a tube of known inner and outer diameter.  
If desired, the tube can be extruded. Once the salt  
10 filled polymer tubes are formed, they are leached in  
water, dissolving the salt crystals and leaving a porous  
network of interconnecting cells 16 as illustrated  
in Fig. 3.

15 This method of formation provides for the rapid and  
reproducible formation of simple geometries within thin  
walled grafts as well as large, intricate geometries within  
thick walled grafts as dictated by the location in which  
the graft is to be utilized. In use, the cardiovascular  
20 graft formed by the method defined above is sutured into  
position to bypass a stenotic region of a blood vessel for  
replacing the naturally occurring blood vessel.

Although the graft 10 of the present invention as  
25 defined above is predominantly used as a cardiovascular  
graft, the graft 10 may also be used alternatively  
as a sewing collar for the fixation of a pervenous  
lead to muscle proximally underlying an area of entry  
of a lead into a blood vessel. Further, the graft 10  
30 may be used as a portion of the insulating material  
on any pacing lead to provide an area of tissue ingrowth  
capability to the lead for purposes of fixing the lead  
in place. Still further, the graft 10 may be used as  
a filter to prevent blockage of catheters by cellular  
35 or proteinaceous debris.

1 It will be apparent from the foregoing description  
that the graft 10 and method for formation of the graft  
10 described above have a number of advantages, some  
of which have been describe above and others of which  
5 are inherent in the invention. For example, the use  
of a non-solvent method in the formation of the graft  
prevents possible physiological reactions of tissue  
to any solvent that might not be leached from the polymer  
in the final steps of forming grafts with a solvent  
10 system. Further, by reaction injection or injection  
molding, there is no limit to the wall thickness which  
can be obtained by the present method.

Also, modifications can be made to the graft and method  
15 of the present invention without departing from the  
teachings of the present invention. Accordingly, the  
scope of the invention is only to be limited as necessitat-  
ed by the accompanying claims.

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## CLAIMS

1. A method for forming a biocompatible polymer graft  
5 particularly adapted for cardiovascular use, said  
method comprising the steps of : choosing a suitable,  
non-solvent, two component, hydrophilic or hydro-  
phobic biocompatible polymer system from which the  
10 graft may be formed; choosing a suitable water soluble  
inorganic salt to be compounded with the biocompatible  
polymer system; grinding the salt crystals and passing  
same through a sieve having a predetermined mesh  
size; drying the salt crystals; compounding the  
15 salt crystals with the biocompatible polymer system;  
forming a tube from said compounded salt and polymer  
system by reaction injection or cast molding; and  
leaching the salt crystals from the formed tube  
with water, said leaching of said salt crystals  
20 providing a tube with a network of interconnecting  
cells formed in the area from which the salt crystals  
have been leached.
2. The method of claim 1 wherein the biocompatible  
polymer system comprises a polymer resin and curing  
25 agent.
3. The method of claim 2 wherein said polymer is chosen  
from the group comprising polyurethane, silicone  
rubber and tetrafluoroethylene.
- 30 4. The method of claim 2 wherein said curing agent  
is chosen from the group comprising platinum, temperat-  
ed steel heat, cross-linkers, gamma radiation and  
ureaformaldehyde.

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- 1 5. The method of claim 1 wherein said inorganic salt  
is chosen to provide cells of predetermined size.
6. The method of claim 6 wherein said inorganic salt  
5 is preferably sodium chloride.
7. The method of claim 1 wherein said salt crystals  
are dried in an oven at a temperature between 100  
and 175°C.
- 10 8. The method of claim 7 wherein said temperature is  
approximately 135°C.
9. The method of claim 1 wherein said crystals are  
15 dried for a minimum of 24 hours.
10. The method of claim 1 wherein said sieve is chosen  
to have a predetermined mesh size.
- 20 11. The method of claim 1 wherein the ratio of water  
soluble inorganic salt to said biocompatible polymer  
system ranges from 25-75% by weight.
12. The method of claim 11 wherein said range is de-  
25 termined by the required flexibility and/or porosity  
of the graft to be fabricated.
13. The method of claim 1 wherein said cells are of  
a uniform diameter within the graft.
- 30 14. The method of claim 1 wherein said cells may vary  
in diameter from graft to graft.
15. The method of claim 1 wherein the diameter of the  
35 cells within the graft is dictated by the location

1 at which the graft is to be used within the cardio-vascular system.

16. The method of claim 1 wherein the wall thickness  
5 of the graft may vary from 5 cm to 4 cm depending on the location at which the graft is to be used in the cardiovascular system.

17. The method of claim 13 wherein the diameter of the  
10 cells in the graft may range from 10 to 200 microns.

18. A graft made by the process of claim 1.

19. A graft particularly adapted for cardiovascular  
15 use, said graft comprising a tube which has been reaction injection molded, cast molded, or extruded from a non-solvent, two component hydrophilic or hydrophobic biocompatible polymer system and which has a honeycomb of interconnecting cells throu-  
20 out the thickness of its wall formed by the leaching of a compounded inorganic salt therefrom.

20. The graft of claim 19 wherein the biocompatible polymer system is a polymer resin and curing agent.  
25

21. The graft of claim 20 wherein said polymer resin is chosen from the group comprising polyurethane, silicone and tetrafluoroethylene (Teflon).

22. The graft of claim 20 wherein said curing agent  
30 is chosen from the group comprising platinum, tempered steel heat, cross linkers, gamma radiation and ureaformaldehyde.

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- 1 23. The graft of claim 19 wherein said inorganic salt  
is chosen to provide cells of predetermined  
size.
- 5 24. The graft of claim 23 wherein said inorganic salt  
is preferably sodium chloride.
25. The graft of claim 19 wherein said salt crystals  
are dried in an oven at a temperature between 100  
10 and 175°C.
26. The graft of claim 25 wherein said temperature is  
approximately 135°C.
- 15 27. The graft of claim 19 wherein said crystals are  
dried for a minimum of 24 hours.
28. The graft of claim 19 wherein said sieve is chosen  
to have a predetermined mesh size.
- 20 29. The graft of claim 19 wherein the ratio of water  
soluble inorganic salt to said biocompatible polymer  
system ranges from 25-75% by weight.
- 25 30. The graft of claim 29 wherein said range is de-  
termined by the required flexibility and/or porosity  
of the graft to be fabricated.
31. The graft of claim 19 wherein said cells are of  
30 a uniform diameter within the graft.
32. The graft of claim 19 wherein said cells may vary  
in diameter from graft to graft.
- 35 33. The graft of claim 19 wherein the diameter of the  
cells within the graft is dictated by the location  
at which the graft is to be used within the cardiovas-  
cular system.

1 34. The graft of claim 19 wherein the wall thickness  
of the graft may vary from 5 cm to 4 cm depending  
on the location at which the graft is to be used  
within the cardiovascular system.

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35. The graft of claim 31 wherein the diameter of the  
cells in the graft may range from 10 to 200 microns.

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FIG. 1

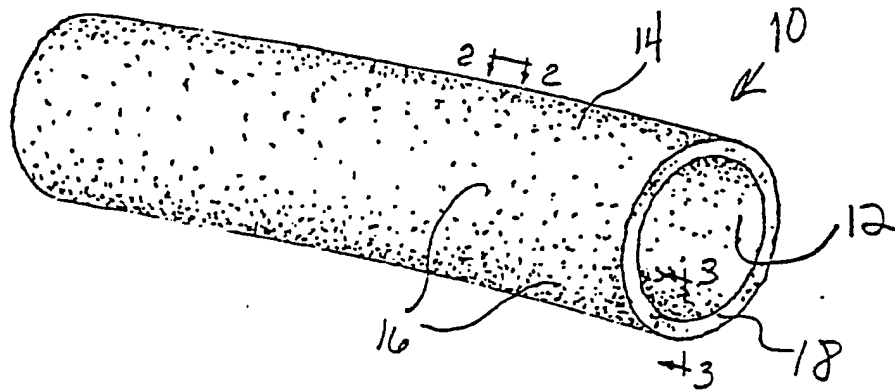


FIG. 2

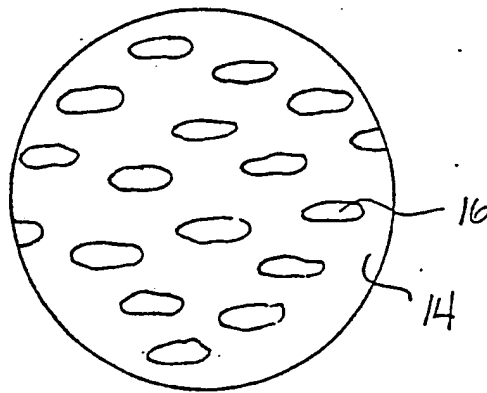


FIG. 3

